ABSTRACT

Charles University in Prague, Faculty of Pharmacy in Hradec Králové

Department of Analytical Chemistry

Candidate: Alena Mikšová

Supervisor: Doc. PharmDr. Lucie Nováková, PhD.

Title of Graduation Thesis:

A development of UHPLC-MS/MS method for the determination of pravastatin, rosuvastatin and their metabolites

This graduation thesis is dealing with the development of UHPLC/MS-MS method for the determination of pravastatin, rosuvastatin and their metabolites. The basic parameters were optimized for MS detection – desolvation temperature, ion optics (RF lens and extractor), nitrogen flow at the sample cone, capillary voltage, nitrogen flow and cone voltage, which is specific for each substance.

Separation of analytes was performed on BEH C18 analytical column (2.1 x 100 mm, 1.7μm). Triple quadrupole was used for detection. Electrospray ionization was performed in both negative and positive mode. Quantification of analytes was performed using the SRM (selected reaction monitoring).

Ion $[M+H]^+$ was chosen for all statins determined in positive ion mode. This ion was the most intense in full scan spectrum. In positive ion mode pravastatin lactone offered also ammonium adduct $[M+NH_4]^+$. All statins determined in negative mode provided a precursor ion $[M-H]^-$. Pravastatin lactone and rosuvastatin lactone offered acetate adduct $[M-H+CH_3COO]^-$ in negative ion mode.

Considering the selected optimal conditions the system suitability test, linearity of the method and its sensitivity were measured. The method was linear. The values of correlation coefficients were in the range from 0.9903 to 0.9986 in positive ion mode and from 0.9954 to 0.9978 in negative ion mode. In positive ion mode limits of detection (LOD) ranged from 0.01 to 0.55 nmol/l and limits of quantitation (LOQ) ranged from 0.03 to 1.87 nmol/l. In negative ion mode limits of detection (LOD) ranged from 0.03 to 524.86 nmol/l and limits of quantitation (LOQ) ranged from 0.11 to 1732.10 nmol/l.

Pravastatin lactone, rosuvastatin lactone and N-desmethyl rosuvastatin provided better results in positive ion mode. Pravastatin and rosuvastatin provide better results in negative ion mode.

Keywords: pravastatin, rosuvastatin, pravastatin lactone, rosuvastatin lactone, N-desmethyl rosuvastatin, UHPLC-MS/MS